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| 09/029,543 | 12/08/98 | RACHAMAN | E 3103/44139 |

HM22/0827
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EXAMINER

OWENS JR, H

| ART UNIT | PAPER NUMBER |
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1623

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DATE MAILED:

08/27/99

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.
09/029,543

Applicant(s)
Rachaman et al

Examiner
Howard Owens

Group Art Unit
1623



☐ Responsive to communication(s) filed on _____.

☐ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) 1-14 is/are pending in the application.

Of the above, claim(s) _____ is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) 1-14 is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☒ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☒ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☒ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

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DETAILED ACTION

5 This application currently names joint inventors. In
considering patentability of the claims under 35 U.S.C. 103(a),
the examiner presumes that the subject matter of the various
claims was commonly owned at the time any inventions covered
therein were made absent any evidence to the contrary. Applicant
is advised of the obligation under 37 CAR 1.56 to point out the
10 inventor and invention dates of each claim that was not commonly
owned at the time a later invention was made in order for the
examiner to consider the applicability of 35 U.S.C. 103[®] and
potential 35 U.S.C. 102(f) or (g) prior art under 35
U.S.C. 103(a).

Claim Objections

Claim 1 appears to contain the misspelled word "oligosacharide".
Claims 1 and 4 appear to contain the misspelled word
"polysacharides".

20 Appropriate correction is required for these and any other
spelling or grammatical errors not noted herein.

Minor informalities

25 The disclosure is objected to because of the following
informalities:

30 p.6, no.11, appears to contain the misspelled word
"Polysocharides".

35 Appropriate correction is required for this and any other
spelling or grammatical errors not noted herein.

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Claim Rejections - 35 USC § 112

5 The following is a quotation of the first paragraph of 35 U.S.C. § 112:

10 The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

15 Claim 14 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

20 Claim 14 is drawn to a pharmaceutical combination of the 3-substituted pyridinium compound together with nicotinic and/or muscarinic and/or glutamate antagonists.

25 The instant specification invites the skilled artisan to experiment. The factors which must be considered in determining undue experimentation are set forth in In re Wands 8USPQ 2d 1400. The factors include:

- 30 1) quantity of experimentation necessary,
2) the amount of guidance presented,
3) the presence or absence of working examples,
4) the nature of the invention,
5) the state of the prior art,
6) the predictability of the art,
35 7) breath of the claims and the
8) level of skill in the art.

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An inventor should be allowed to dominate future patentable inventions of others where those inventions were based in some way on his teachings, since such improvements, while unobvious from his teachings, are still within his contribution, since
5 improvement was made possible by his work; however, he must not be permitted to achieve this dominance by claims which are insufficiently supported and, hence, not in compliance with first paragraph of 35 U.S.C. 112.

10

As the instant claim is drafted as a composition claim, applicant should provide adequate representation of the claim
15 pyridinium compound(s) in combination with nicotinic and/or muscarinic and/or glutamate antagonists. However, there is not seen sufficient representation in the instant specification
20 wherein a 3-substituted pyridinium compound is combined with nicotinic, muscarinic and glutamate antagonists as one composition, nor wherein the 3-substituted pyridinium compound is combined with a lone antagonist. Without adequate representation to establish dosage and effective concentrations of the
25 pyridinium compound and the antagonist, one of skill in the art would be faced with undue experimentation in the practice of the instantly claimed composition.

30

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject
35 matter which the applicant regards as his invention.

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Claims 1-14 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant
5 regards as the invention.

In claim 1, use of the term "general" renders the claim
10 indefinite, as the structure can be no more general than which is specifically set forth in the claim and associated Markush groups. Accordingly, dependent claims 2-4 are rejected as they fail to obviate the rejections set forth in the parent claim(s).

A broad range or limitation together with a narrow range or
15 limitation that falls within the broad range or limitation (in the same claim) is considered indefinite, since the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. Note the explanation given by the Board of Patent Appeals and Interferences in *Ex parte Wu*, 10
20 USPQ2d 2031, 2033 (Bd. Pat. App. & Inter. 1989), as to where broad language is followed by "such as" and then narrow language. The Board stated that this can render a claim indefinite by raising a question or doubt as to whether the feature introduced by such language is (a) merely exemplary of the remainder of the

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claim, and therefore not required, or (b) a required feature of the claims. Note also, for example, the decisions of *Ex parte Steigewald*, 131 USPQ 74 (Bd. App. 1961); *Ex parte Hall*, 83 USPQ 38 (Bd. App. 1948); and *Ex parte Hasche*, 86 USPQ 481 (Bd.

5 App. 1949). In the present instance, claim 1 recites the broad recitation aldoses, and the claim also recites aldohexoses, which is the narrower statement of the range/limitation. Claim 4 also recites the following broad recitations deoxyhexose, alditol, cyclohexitol, disaccharide, amino sugar and the claim
10 also recites fucose, mannitol, or mannose; dulcitol, rebitol, erythritol and glycerol; inositol and myoinositol; lactose, maltose and sucrose; glucoseamine and N-acetylglucosamine which are the respective narrower statements of the range/limitation. Accordingly, dependent claims 2-4 are rejected as they fail to
15 obviate the rejections set forth in the parent claim(s).

In claim 5, applicant sets forth a composition however only one component, a compound is set forth, as a valid composition claim requires at least two components, claim 5 is indefinite. Accordingly, dependent claims 6-14 are rejected as they fail to
20 obviate the rejections set forth in the parent claim(s).

Claim 9 is a duplicate of claim 5. Given that intended use of a composition does not carry patentable weight, applicant has merely set forth a duplicate of the composition found in parent claim 5.

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In claim 10, applicant sets forth a method of treatment however as the instant claim is drafted it is unclear as to how the method is to be carried out. Applicant sets forth a method of treatment and pretreatment comprising an effective amount, but there is no mention of administration or route of administration. Moreover, the use of parenthetical phrasing "(neurogenic urine bladder)" renders the claim indefinite.

In the absence of structures or classes of compounds, the term "biodegradable polysaccharide" in claim 12 is vague and indefinite.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. § 103 which forms the basis for all obviousness rejections set forth in this Office action:

A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Subject matter developed by another person, which qualifies as prior art only under subsection (f) or (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention

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were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.

5

Claims 1-13 are rejected under 35 U.S.C. § 103 as being unpatentable over Bodor, U.S. Patent No. 4,824,850 and Naito, JP 05339148 A2 (abstract).

10

Claims 1-7 are drawn to a 3-substituted pyridinium compound and composition thereof, wherein a sugar moiety is attached to facilitate passage of the compound through the blood brain barrier (BBB).

15

Claims 8-13 are drawn to a method of treating cholinergic disorders, glaucoma, myasthenia gravis, pretreatment of organophosphorous intoxication and treatment of urine bladder dome.

20

Bodor teaches the use of pyridinium derivatives and associated salts for the delivery of pharmaceuticals through the BBB. Bodor teaches that pyridinium derivatives and associated salts provide a generic method for specific and/or target enhanced delivery to the brain of a wide variety of centrally acting drug species (col. 5-col.7). Bodor also teaches the conjunction of these substituted pyridinium salts with sugars (col. 209-210). Bodor however does not teach a pyridinium compound identical to that set forth by applicant in the instant claims.

25

30

Naito teaches the use of sugars to allow pharmaceuticals to pass through the blood brain barrier. Sugars such as galactose, lactose, glucose, arabinose, fructose, maltose, glucosamine, mannosamine and galactosamine.

A prima facie case of obviousness is supported when the prior art alone would have appeared to suggest doing, at the time the invention was made, what the applicant

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has done. Although, the exact pyridinium compound is not disclosed in Naito or Bodor, one of skill in the art would have been provided with a with a clear motivation and a reasonable expectation of success link a glycosyl moiety to the claimed pyridinium compound as the presence of sugars have been shown to facilitate the passage of
5 pharmaceuticals through the BBB.

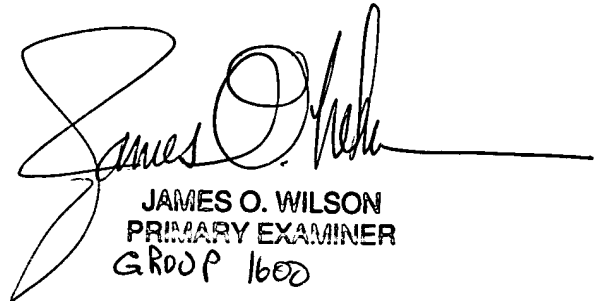
A patentable compound or composition of matter is one that is produced by intermixture of two or more specific ingredients; and possesses properties pertaining to none of these ingredients separately, thereby accomplishing a new and useful result. Both
10 substituted pyridinium derivatives and sugars have been shown to be agents which can successfully pass through the blood brain barrier as lone agents or in combination with other pharmaceuticals. Therefore, it would have been obvious to modify the teachings of Bodor in view of Naito to include sugars or
15 glycosyl moieties in a pharmaceutical composition to enhance delivery of a pharmaceutical wherein the treatment of CNS, cholinergic disorders and the like is reliant upon passage of these compounds through the BBB. One of skill in the art would also expect the compounds to be beneficial in the treatment of
20 the alleviation of side-effects induced by antimuscarinic tricyclic antidepressants, symptoms of peripheral cholinergic disorders, glaucoma, myasthenia gravis and the pretreatment of organophosphorous intoxication as substituted pyridinium compounds of this general formula (such as physostigmine,
25 pyridostigmine and neostigmine) have been known in the art to display these pharmacological properties and therapeutic uses.

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to Howard Owens whose telephone number is (703) 306-4538 . The examiner can normally be reached on Mon.-Fri. from 8:30 a.m. to 5 p.m.

5 If attempts to reach the examiner by telephone are unsuccessful, the Primary Examiner signing this action, James O. Wilson can be reached on (703) 308-4624 . The fax phone number for this Group is (703) 308-4556.

10 Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-1235.



JAMES O. WILSON
PRIMARY EXAMINER
GROUP 1600